

#34  
*Appeal Brief*  
1642

APPEAL BRIEF  
-EXPEDITED PROCEDURE-  
ART UNIT: 1642

Express Mail Label No: EL 926059630 US  
Date of Deposit: August 15, 2003

ATTORNEY'S DOCKET NO: S01237.70011.US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Kenneth Walsh  
Serial No : 09/408,905  
Conf. No : 4597  
Filed : September 29, 1999  
For : AKT COMPOSITIONS FOR ENHANCING SURVIVAL OF CELLS  
Examiner : Nickol, G.  
Art Unit : 1642

Mail Stop Appeal Brief - Patents  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

RECEIVED

AUG 20 2003

TECH CENTER 1600/2900

APPELLANT BRIEF

08/19/2003 MBIZUNES 00000010 09408905  
02 FC:1402 320.00 OP

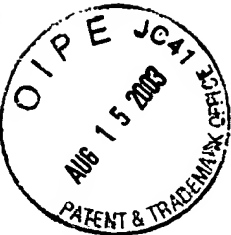
Helen C. Lockhart  
Reg. No. 392,248  
WOLF, GREENFIELD & SACKS, P.C.  
600 Atlantic Avenue  
Boston, MA 02210-2211  
(617) 720-3500  
Attorneys for Appellant

## TABLE OF CONTENTS

	<u>Page</u>
I. Real Party in Interest (37 C.F.R. §1.192(c)(1)).....	1
II. Related Appeals and Interferences (37 C.F.R. §1.192(c)(2)).....	1
III. Status of Claims (37 C.F.R. §1.192(c)(3)) .....	1-2
A. Total Number of Claims in Application	
B. Status of All the Claims	
C. Claims on Appeal	
IV. Status of Amendments (37 C.F.R. §1.192(c)(4)) .....	2
V. Summary of Invention (37 C.F.R. §1.192(c)(5)) .....	2-3
VI. Issues (37 C.F.R. §1.192(c)(6)).....	3
VII. Grouping of Claims (37 C.F.R. §1.192(c)(7)).....	3
VIII. Argument (37 C.F.R. §1.192(c)(8)(iv)).....	3-11
IX. Conclusion.....	11-12
Appendix A: Claims As Appealed (37 C.F.R. §1.192(c)(9)) .....	13

**TABLE OF CASES AND CITED AUTHORITIES**  
*(In order of appearance)*

1.	Cuevas P et al., Fibroblast growth factor-1 prevents myocardial apoptosis triggered by ischemia reperfusion injury. <u>Eur. J. Med. Res.</u> 1997 Nov 28;2(11):465-8.....	3
2.	Datta SR et al., Akt phosphorylation of BAD couples survival signals to the cell-intrinsic death machinery. <u>Cell.</u> 1997 Oct 17;91(2):231-41.....	3
3.	<u>Sensonics, Inc. v. Aerosonic Corp.</u> , 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996).....	10
4.	<u>In re Zurko</u> , 111 F.3d 887, 42 USPQ2d 1476 (Fed. Cir. 1997) .....	10
5.	<u>In re Vaeck</u> , 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) .....	5
6.	<u>W.L. Gore &amp; Assocs., Inc. v. Garlock, Inc.</u> , 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).....	10



This brief, submitted in triplicate, is in furtherance of the Notice of Appeal filed in this case on January 15, 2003.

The fees required under 37 C.F.R. §1.17(c) are dealt with in the accompanying Transmittal of Appeal Brief.

**I. REAL PARTY IN INTEREST (37 C.F.R. §1.192(c)(1))**

The real party in interest in this matter is Caritas Saint Elizabeth's Medical Center of Boston, Incorporated, the successor in name to the Assignee of current record, St. Elizabeth's Medical Center. The above-named inventor Kenneth Walsh assigned all his rights in the invention to St. Elizabeth's Medical Center on December 13, 1999, in an Assignment recorded in the United States Patent and Trademark Office on January 6, 2000, at Reel 010590, Frame 0406.

**II. RELATED APPEALS AND INTERFERENCES (37 C.F.R. §1.192(c)(2))**

The undersigned appellant's legal representative avers that to the best of his/her knowledge and belief, there are no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

**III. STATUS OF CLAIMS (37 C.F.R. §1.192(c)(3))**

This Appeal involves all of the claims pending in the application, claims 1-5. Claims 1-4 stand finally rejected under 35 U.S.C. § 103 (a), and claim 5 stand objected to by the Examiner as dependent upon a rejected base claim.

**A. TOTAL NUMBER OF CLAIMS IN APPLICATION**

Claims in the application are: 1-38

**B. STATUS OF ALL THE CLAIMS**

- |  |      |
|--|------|
| 1. Claims canceled:                    | -0-  |
| 2. Claims withdrawn from consideration |      |
| but not canceled:                      | 6-38 |
| 3. Claims pending:                     | 1-5  |
| 4. Claims allowed:                     | None |

5. Claims rejected:

1-5

**C. CLAIMS ON APPEAL**

Claims 1-5 are reproduced in Appendix A.

**IV. STATUS OF AMENDMENTS (37 C.F.R. §1.192(C)(4))**

A Response After Final mailed January 15, 2003, in response to the Office Action made final and mailed July 15, 2002 (Paper No. 25), has been considered by the Examiner and discussed in an Advisory Action mailed February 26, 2003 (Paper No. 32). No amendments to the claims have been made. The original claims as filed are pending.

**V. SUMMARY OF INVENTION (37 C.F.R. §1.192(C)(5))**

The claimed invention relates generally to the discovery by the inventor that certain Akt molecules can be used to inhibit death of heart tissue. More specifically, the invention relates to methods of using certain Akt molecules to inhibit death of heart muscle cells (cardiomyocytes) and cardiac endothelial cells. Such methods are useful, for example, for treating myocardial infarction in a subject (page 18, line 17 – page 19, line 9).

Claim 1 is directed to a method for treating myocardial infarction comprising administering to a subject in need of such treatment an Akt molecule in an amount effective to inhibit cardiac tissue necrosis in the subject. Support for this claim can be found throughout the specification, including page 2, lines 23-30; page 7, lines 2-8; page 18, line 17 – page 19, line 9; page 21, lines 24-27; page 22, lines 2-5; and Example 4, beginning at page 48 and especially page 53, line 17 – page 54, line 10. An Akt molecule as claimed embraces both Akt nucleic acids and Akt polypeptides (page 7, lines 26-27), as those terms are disclosed at page 7, line 30 – page 13, line 6, and at page 16, line 25 – page 18, line 16, respectively. Akt molecules specifically include, without limitation, both wild-type and constitutively active forms of Akt molecules (page 2, lines 31-32; page 8, lines 24-32; page 18, lines 6-16; page 19, lines 16-18).

Claim 2 is directed to the method of claim 1, wherein the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a cardiomyocyte. Support for this claim can be

found throughout the specification, including as described above with reference to support for claim 1, as well as at page 3, lines 10-11.

Claim 3 is directed to the method of claim 1, wherein the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a vascular endothelial cell. Support for this claim can be found throughout the specification, including as described above with reference to support for claim 1, as well as at page 3, lines 11-12, and at page 20, lines 9-15.

Claim 4 is directed to the method of claim 1, wherein the Akt molecule is administered acutely. Support for this claim can be found throughout the specification, including as described above with reference to support for claim 1, as well as at page 3, line 7, and at page 21, line 32 – page 33, line 5.

Claim 5 is directed to the method of claim 4, wherein the Akt molecule is administered acutely into the apical and anterolateral free wall of the heart. Support for this claim can be found throughout the specification, including as described above with reference to support for claim 4, as well as at page 3, lines 8-9, and in Example 4, particularly at page 53, lines 22-24.

#### **VI. ISSUES PRESENTED FOR REVIEW ON APPEAL (37 C.F.R. §1.192(c)(6))**

Whether claims 1-4 are unpatentable under 35 U.S.C. § 103(a) over Cuevas et al. in view of Datta et al.

#### **VII. GROUPING OF CLAIMS (37 C.F.R. §1.192(c)(7))**

For the purposes of this Appeal only, all claims stand or fall together.

#### **VIII. ARGUMENT (37 C.F.R. §1.192(c)(8)(iv))**

The Appellant respectfully requests that the Examiner's final rejection of all of the claims be reversed. The claims as presented are believed to be in allowable condition. Claims 1-4 were finally rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Cuevas et al. (Eur. J. Med. Res. 2:465-8, 1997) in view of Datta et al. (Cell, 91:231-41, 1997). Appellant respectfully appeals this rejection for the reasons set forth below. In short, Appellant takes the

position that the Examiner has failed to make a prima facie case for making the obviousness rejection here at issue.

The claims on appeal are directed to a method for treating myocardial infarction comprising administering to a subject an Akt molecule in an amount effective to inhibit cardiac tissue necrosis (Claim 1). The dependent claims further specify that the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a cardiomyocyte (Claim 2) wherein the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a cardiac tissue endothelial cell (Claim 3) and wherein the Akt molecule is administered acutely (Claim 4).

The rejection as originally made in Paper No. 13 and maintained in Paper No. 16, Paper No. 21 (vacated by the Examiner in Paper No. 25), and the Advisory Action of Paper No. 32, is as follows. According to the Examiner, Cuevas et al. teach a method for treating myocardial infarction that involves administering to a subject in need of such treatment a molecule (i.e., fibroblast growth factor-1, FGF-1) in an amount effective to inhibit cardiac tissue necrosis (abstract) wherein the cardiac tissue necrosis is mediated by increased apoptotic cell-death of a cardiomyocyte (introduction and page 466, 1st column) and a cardiac tissue endothelial cell (Fig. 1, page 467) wherein the molecule is also administered acutely (abstract).

The Examiner acknowledges that the Cuevas et al. reference does not disclose an Akt molecule in the treatment protocol.

However, the Examiner further states that the Datta et. al. reference teaches that the Akt molecule is an inhibitor of apoptosis in “a variety of cell types (page 231, 2nd column, 2nd full paragraph).” The Examiner concludes that it would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to “substitute the apoptotic inhibitor used by Cuevas et al. with the Akt molecule taught by Datta et al. in order to treat a myocardial infarction because both molecules are well known in the art to function as inhibitors of apoptosis.” The Examiner further states that based on the Datta et al. teachings, one skilled in the art would have expected that an Akt molecule would also treat a myocardial infarction. The Examiner relies on the Cuevas et al. reference for motivation to make this substitution because Cuevas et al. “successfully teach that when FGF was given as a systemic bolus immediately after myocardial ischemia, apoptosis was significantly reduced by 60%.” In conclusion, the Examiner states that

730514

since both molecules, i.e., FGF-1 and Akt, function to inhibit apoptosis, “it would have been obvious to one of ordinary skill in the art to use an Akt molecule to treat myocardial infarctions.”

#### Response

Appellant traverses the Examiner’s conclusion that one of ordinary skill in the art would have been motivated to substitute the Akt molecule as taught by Datta et al. for the FGF-1 molecule as taught by Cuevas et al. to result in the invention as claimed. The Examiner correctly acknowledges that the Cuevas et al. reference does not teach or suggest the use of an Akt molecule for treating myocardial infarction. The only purported nexus between the Cuevas et al. and the Datta et al. references is that each relates, in a *general* sense, to an apoptotic process.

As set forth in MPEP §2143, three criteria must be met in order to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited references or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to modify the reference, or to combine reference teachings, and the reasonable expectation of success must both be found in the prior art, and not based on Appellant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

#### The Examiner has failed to make a prima facie case for the obviousness rejection

##### 1. One of skill in the art would not have combined the Datta et al and Cuevas et al references because the components of the reference are not simply interchangeable

One of skill in the art would not combine the references with the expectation that Akt would induce apoptosis in cardiomyocytes and cardiac tissue endothelial cells based on the teachings of Cuevas et al. that FGF prevents myocardial apoptosis and the teachings of Datta et al. that Akt induces apoptosis in some unrelated cell types.

730514



a. FGF and Akt are distinct molecules.

Importantly, FGF does not activate Akt in cardiomyocytes, skeletal myocytes, or vascular endothelial cells. Appellant is not aware of a link between FGF and Akt in these cells. Therefore the observation that FGF promotes cardiomyocyte survival says nothing about the role or potential role of Akt in cardiomyocytes, skeletal myocytes, or vascular endothelial cells.

b. The cells described in the two references are distinct

It is widely appreciated that differentiated cells from various tissues are structurally and functionally dissimilar. Because neurons and cardiac myocytes are so plainly distinct in their structure and function, one of skill in the art would not expect that a compound that induces apoptosis in one cell type would necessarily have the same effect in another cell type, in the absence of any further information linking the apoptotic pathways of the cells or analyzing expression and/or activity of the compound in the cells. Thus, one of skill in the art would not expect that Akt, an apoptosis inhibitor reported to be effective in neurons, would be effective in cardiac myocytes, in the absence of further scientific evidence.

c. The rejection is not sufficient because the teachings of references are not interchangeable

The Examiner relies upon the Datta et al. reference for showing that an “Akt molecule is an inhibitor of apoptosis in a variety of cell types.” Paper No. 13, page.5. This reliance is misplaced. Datta et al. does not teach, suggest, or render obvious that Akt would be expressed in the types of cells which play a critical role in myocardial infarction. The paragraph cited by the Examiner for support that Datta teaches an Akt molecule as an inhibitor of apoptosis in a variety of cell types is quoted below in its entirety. (page 231, second column, second full paragraph):

Akt is a general mediator of growth factor-induced survival and has been shown to suppress the apoptotic death of a number of cell types induced by a variety of stimuli, including growth factor withdrawal, cell-cycle discordance, loss of cell adhesion, and DNA damage (Ahmed et al., 1997; Dudek et al., 1997; Kauffmann-

Zeh et al., 1997; Kennedy et al., 1997; Khwaja et al., 1997; Kulik et al., 1997). Thus, a signaling pathway has been defined in which growth factor receptor activation leads to the sequential activation of PI3'K and Akt, which then, through as-yet undescribed mechanisms, promotes cell survival and blocks apoptosis.<sup>1</sup>

Significantly, none of the references cited in the above-quoted paragraph from Datta et al. teach or suggest the expression of Akt in the cell types which are the subject of the pending application. As stated on page 2 of the specification (emphasis added),

...Activation of Akt reportedly inhibits apoptosis induced by growth factor withdrawal or irradiation in neural cells, fibroblasts, and lymphocytes (Franke, T.F., et al., *Science*, 1997, 275:665-668; Hemmings, *Science*, 1997, 275:628-630). ...

The invention involves the discovery that Akt ... inhibits apoptotic cell-death of cardiomyocytes, skeletal myocytes and/or vascular endothelial cells. In view of these discoveries, it is believed that Akt molecules can be used to inhibit apoptotic cell-death of the afore-mentioned cell types, and in particular, to treat conditions (e.g., myocardial infarction) that result in increased apoptotic cell-death of cardiomyocytes, skeletal myocytes and/or vascular endothelial cells.

The expression of Akt in one cell type would not lead one of ordinary skill in the art to have a reasonable expectation that Akt would be expressed in a completely different cell type and in response to different and more complex stimuli, e.g., ischemia and ischemia-reperfusion injury which involves the accumulation of metabolic waste products, changes in mechanical factors and the generation of toxic substances. Accordingly, Appellant's discovery of the expression of Akt in cardiomyocytes and cardiac tissue endothelial cells and the use of this discovery to treat conditions that are mediated by expression of Akt in these cell types is neither taught nor suggested by the prior art teachings that Akt is expressed in neural cells, fibroblasts, and lymphocytes. In contrast to the cited art, each of the pending claims is directed to achieving

---

<sup>1</sup> The exact cell types involved in the string citation are: BAF/3 (IL-3-dependent lymphoid cell line) and 2780a (IL-2-dependent T cell line) (Ahmed et al.); neurons (Dudek et al.); fibroblasts (Kauffman-Zeh et al., Kennedy et al., and Kulik et al.); and epithelial cells (Khwaja et al.).

increased Akt expression in the specific cell types which were the subject of Appellant's discovery.

In summary, the Examiner has failed to make a prima facie case for the obviousness rejection because expression of Akt in non-cardiac cells in response to certain stimuli would not suggest to one of ordinary skill in the art that Akt would be expressed in cardiomyocytes and cardiac tissue endothelial cells and in response to different stimuli.

2. There would be no reasonable expectation of success for combining the Datta et al and Cuevas et al references because there is more than one apoptotic pathway and not all apoptosis inhibitors are alike

a. Multiple apoptotic pathways exist

There are many reports in the literature of Akt-independent cellular survival, showing that not all apoptotic or anti-apoptotic stimuli funnel through this regulatory pathway. Furthermore, it is clear that there are diverse intracellular mechanisms that promote cell death. In the broadest sense, in apoptosis there is an "intrinsic" cell death pathway and an "extrinsic" cell death pathway. The intrinsic pathway functions through the mitochondria and is largely sensitive to Akt. In contrast, the extrinsic pathway involves Fas ligand and caspase 8, and is largely insensitive to Akt. In addition, caspase-independent apoptosis is also understood at this time. This latter process involves AIF (apoptosis-inducing factor), but apparently not Akt. Therefore methods directed to protecting against apoptosis are expected to be heterogeneous because it appears that apoptosis itself is heterogeneous in nature.

The teachings of Datta et al. and of Cuevas et al. do not suggest that the cell death pathway in myocardial infarction or in ischemia-reperfusion injury involves the intrinsic cell death pathway. Datta et al. teaches that Akt-mediated cell survival is mediated by the ability of Akt to phosphorylate and thereby inactivate BAD, a pro-apoptotic protein relevant to the intrinsic cell death pathway. This mechanism, as taught by Datta et al., therefore is applicable only to the intrinsic cell death pathway. There is no teaching or suggestion in either Datta et al. or Cuevas et al. that the cell death pathway in myocardial infarction or in ischemia-reperfusion

730514

injury involves the intrinsic cell death pathway. Indeed, the teaching of Cuevas et al., alone or in combination with Datta et al., supports an opposite conclusion, because (i) Cuevas teaches the beneficial effects of FGF-1, a growth factor known not to act through Akt, and (ii) Datta et al. teaches that BAD-independent survival mechanisms likely also exist (Datta, caption for Figure 8). Taken together, Datta et al. and Cuevas et al. suggest that FGF-1 and Akt are not interchangeable, as suggested by the Examiner, because FGF-1 may act through a pathway that has no connection to Akt or BAD. It therefore would not have been obvious at the time the invention was made to substitute Akt for FGF-1 in order to arrive at the claimed invention.

In summary, one of skill in the art would not have a reasonable expectation of success in combining the two references as suggested by the examiner because at the time the invention was made it was not known if the teachings of the cited references relate to the same or different apoptotic cell death pathways.

b. Not all apoptosis inhibitors are alike.

Even among growth factors thought to be survival factors, e.g., apoptosis inhibitors, it is unreasonable to suggest that one apoptosis inhibitor can arbitrarily be substituted for another. For example, growth factors for the most part act through specific cell surface receptors. Platelet-derived growth factor (PDGF), nerve growth factor (NGF), and insulin-like growth factor-1 (IGF-1) each have their own specific receptors. Thus while neurons expressing NGF receptor may be responsive to NGF, other cell types not expressing NGF receptor would not be expected to be responsive to NGF. Conversely, cells expressing receptors for PDGF, NGF, and IGF-1 may not be responsive to another growth factor for which there is little or no expression of receptors specific for that growth factor. Furthermore, individual growth factors and their receptors may invoke different and non-intersecting intracellular signaling pathways. As discussed above, Datta et al. teach that Akt is involved in inhibiting the intrinsic cell death pathway. There is no specific teaching or suggestion in Datta or Cuevas that FGF-1 acts through the intrinsic cell death pathway. It is therefore untenable to suppose that for any given cell type, one apoptosis inhibitor can arbitrarily be substituted for another. In particular, it is therefore untenable to suppose that for cardiac tissue, Akt can arbitrarily be substituted for FGF-1.

730514

### Improper Use of Hindsight

The Examiner's rejection under 35 U.S.C. §103(a) is a classic example of an impermissible use of hindsight. For the rejection under 35 U.S.C. §103(a) presented in the Final Office Action, the Examiner explicitly drew on the teachings of Appellant's application to provide the suggestion or motivation for combining the cited references to arrive at the claimed invention.

It is improper for the Examiner to draw on such hindsight knowledge of the present invention when the prior art does not contain or suggest that knowledge. The present invention may not be used as a template for its own reconstruction. Sensonic, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996). "The invention must be viewed not after the blueprint has been drawn by the inventor, but as it would have been perceived in the state of the art that existed at the time the invention was made." Id. "To imbue one of ordinary skill in the art with knowledge of the invention...when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher." In re Zurko, 111 F.3d 887, 42 USPQ2d 1476 (Fed. Cir. 1997) (quoting W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983)).

As discussed in detail further below, without Appellant's disclosure the Examiner can point to no teaching in the prior art that would motivate one of ordinary skill to modify any reference or combination of references to arrive at the claimed invention. Furthermore, the Examiner has not referenced any general knowledge of one of ordinary skill in the art for such a teaching. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness.

The only reason to combine Datta et al with Cuevas et al is a desire to produce the claimed invention -- something that no one in the art appears to have done before the Appellant. Without any suggestion or motivation provided by either general knowledge of one skilled in the art or any specific teaching in the prior art, and relying only upon Appellant's disclosure, such an exercise amounts to an improper and impermissible use of hindsight.

Appellant has discovered that Akt inhibits the death of heart tissue, in particular cardiomyocytes and cardiac endothelial cells. It is this teaching that forms the basis for the combination of references. In the absence of this teaching one of skill in the art would not combine the references in the manner set forth by the examiner, for the reasons described above. It is only with the use of impermissible hindsight (knowing that Akt inhibited apoptosis in heart tissue) that one of skill in the art would have used Akt to inhibit apoptosis in heart tissue.

According to the Examiner, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to “substitute the apoptotic inhibitor used by Cuevas et al. [FGF-1] with the Akt molecule taught by Datta et al. in order to treat a myocardial infarction because both molecules are well-known in the art to function as inhibitors of apoptosis” (Paper No. 13, page 5). Based on this rationale for the obviousness rejection, one would necessarily conclude that one skilled in the art would have been motivated to substitute any apoptosis inhibitor for FGF-1 for treating any disease which involved apoptotic cell death. The mere nexus that FGF-1 is an apoptosis inhibitor is: (1) insufficient to motivate one skilled in the art to select Akt over other apoptosis inhibitors that were available at the time the invention was made; and (2) insufficient to provide one skilled in the art with a reasonable expectation of success that the selected Akt would be useful for treating disorders mediated by apoptotic cell death in cardiomyocytes and/or cardiac tissue endothelial cells.

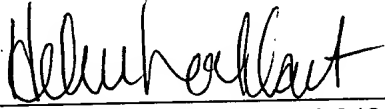
In summary, the generic basis offered by the Examiner for rejecting the claimed invention lacks the particular findings of fact to support a prima facie showing of non-obviousness.

## **IX. CONCLUSION**

In view of the foregoing, Appellant respectfully requests that the Board of Appeals reconsider and withdraw the Examiner’s final rejection of claims 1-4 under 35 U.S.C. § 103(a). Appellant further requests that the objection to claim 5 as being dependent on a rejected base claim also be withdrawn upon withdrawal of the rejection of claims 1-4.

It is believed that the Examiner has not made out a prima facie basis for rejecting the claims and that the claims are allowable over the prior art of record. It is requested that the rejection be reversed and that a Notice of Allowance be granted in this case.

Respectfully submitted,

By: 

Helen C. Lockhart, Reg. No. 39,248  
Wolf, Greenfield & Sacks, P.C.  
600 Atlantic Avenue  
Boston, MA 02210  
Tel. (617) 720-3500

Docket No. S01237.70011.US  
Filed: August 15, 2003  
**xx08/15/03xx**

**APPEAL BRIEF  
-EXPEDITED PROCEDURE-  
ART UNIT: 1642**

**Express Mail Label No: EL 926059630 US  
Date of Deposit: August 15, 2003**

ATTORNEY'S DOCKET NO: S01237.70011.US

**Appendix A: Claims As Appealed (37 C.F.R. §1.192(c)(9))**

1. (original) A method for treating myocardial infarction comprising:  
administering to a subject in need of such treatment an Akt molecule in an amount  
effective to inhibit cardiac tissue necrosis in the subject.
2. (original) The method of claim 1, wherein the cardiac tissue necrosis is mediated by  
increased apoptotic cell-death of a cardiomyocyte.
3. (original) The method of claim 1, wherein the cardiac tissue necrosis is mediated by  
increased apoptotic cell-death of a cardiac tissue endothelial cell.
4. (original) The method of claim 1, wherein the Akt molecule is administered acutely.
5. (original) The method of claim 4, wherein the Akt molecule is administered acutely into  
the apical and anterolateral free wall of the heart.